REMARKS

Claims 1-64 were pending. Claims 31 and 46 have been cancelled. Claims 28, 29, 32, 47, 52, 53, and 58 have been amended. Therefore, claims 1-30, 32-45, and 47-64 are pending.

No new matter has been added. Claims 28, 29, 32, 47, 52, 53, and 58 have been amended to clarify the invention.

Rejection of Claims 28-30 under 35 U.S.C. § 112, second paragraph

Claims 28-30 are rejected under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention."

Applicants respectfully submit that the language objected to by the Examiner is no longer recited in the claims as currently amended. Therefore, Applicants respectfully request that this rejection of claims 28-30 under 35 U.S.C. § 112, second paragraph be withdrawn.

Provisional Rejection of Claims 10-15 and 17-29 under 35 U.S.C. § 101

Claims 10-15 and 17-29 are rejected under 35 U.S.C. § 101 "as claiming the same invention as that of claims 3-9, 11-17, 19-23, 25 and 29 of copending Application No. 09/882,273."

Applicants submit that the claims 10-15 and 17-29 of the instant application are directed to compositions which are 7-substituted tetracycline compound and substantially free of positional isomers. The compositions claimed in claims 3-9, 11-17, 19-23, 25 and 29 of U.S.S.N. 09/882,273 are not directed to compositions which are substantially free of positional isomers. Therefore, Applicants respectfully request that this rejection of claims 10-15 and 17-29 under 35 U.S.C. § 101, be withdrawn.

Provisional Rejection of Claims 3, 5, 7, 9, 31 and 39 under 35 U.S.C. § 101

Claims 3, 5, 7, 9, 31 and 39 are rejected under 35 U.S.C. § 101 "as claiming the same invention as that of claims 3, 6, 8, 10, 29 and 30 of copending Application No. 09/882,505." Claim 31 has been cancelled, thus rendering its provisional rejection moot.

Applicants submit that the claims 3, 5, 7, 9 and 39 of the instant application are directed to compositions which are 7-substituted tetracycline compound and substantially free of positional isomers. The compositions claimed in claims 3, 6, 8, 10, 29 and 30 of U.S.S.N. 09/882,505 are not directed to compositions which are substantially free of

positional isomers. Therefore, Applicants respectfully request that this rejection of claims 3, 5, 7, 9 and 39 under 35 U.S.C. § 101, be withdrawn.

Provisional Rejection of Claims 1, 2, 4, 6, 8, 10-30, 32-38, and 40-45 under the Judicially Created Doctrine of Obviousness-Type Double Patenting

Claims 1, 2, 4, 6, 8, 10-30, 32-38, and 40-45 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of copending Application No. 09/882,273.

Applicants note that U.S. Application No. 09/882,273 has not yet issued as a patent and, therefore, the double patenting rejections are provisional. Applicants will address the double patenting issue upon a finding of subject matter in the instant application that is allowable but for the double patenting rejection.

Provisional Rejection of Claims 1-9 and 31-64 under the Judicially Created Doctrine of Obviousness-Type Double Patenting

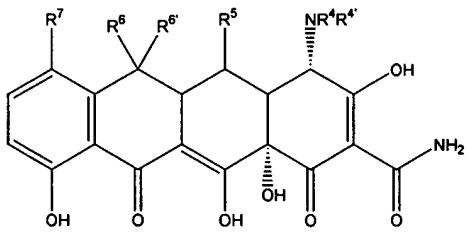
Claims 1-9 and 31-64 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-31 of copending Application No. 09/882,505.

Applicants note that U.S. Application No. 09/882,505 has not yet issued as a patent and, therefore, the double patenting rejections are provisional. Applicants will address the double patenting issue upon a finding of subject matter in the instant application that is allowable but for the double patenting rejection.

Rejection of Claims 1-4, 8, 9, 24-30 and 58-64 under 35 U.S.C. § 102(b)

Claims 1-4, 8, 9, 24-30, and 58-64 are rejected under 35 U.S.C. § 102(b) as being anticipated by Koza, *J. Am. Chem. Soc.*, 2(6), 815-17, 2000 ("Koza").

Claims 1-4, 8, 9, and 24-30 are directed to 7-substituted tetracycline compounds which are substantially free of positional isomers, having the formula:



(I)

wherein:

R^4 and $R^{4'}$ are each alkyl;

R^5 is hydrogen, hydroxyl, or a prodrug moiety;

R^6 and $R^{6'}$ are each independently hydrogen, hydroxyl, alkyl, or taken together, alkenyl;

R^7 is halo substituted, N-substituted or unsubstituted phenyl, and pharmaceutically acceptable salts thereof, wherein said tetracycline compound is substantially free of positional isomers.

Claims 58-64 are directed, at least in part, to pharmaceutical compositions comprising compounds of formula (I).

Koza describes 7-substituted compounds, synthesized from sancycline, sulfuric acid and N-iodosuccinimide, as described in the supporting information. The products produced in this reaction are a mixture of the 9-iodosancycline positional isomer, the 7-iodosancycline positional isomer, and 7,9-diiodosancycline. Koza does not teach or suggest compositions which are substantially free from positional isomers as claimed by Applicants.

Therefore, Applicants respectfully request that this rejection of claims 1-4, 8, 9, 24-30, and 58-64 under 35 U.S.C. § 102(b), be withdrawn.

Rejection of Claims 1-30, 32-45, and 47-64

Claims 1-30, 32-45, and 47-64 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Koza.

As described above, claims 1-30 and 32-36 are directed to 7-substituted tetracycline compounds of Formula (I), which are substantially free of positional isomers. Claims 37-45 and 47-57 are directed to methods for treating a tetracycline responsive state in a mammal, by administering to the mammal a 7-substituted tetracycline compound of Formula I, which is substantially free of positional isomers. Claims 58-64 are directed to pharmaceutical compositions comprising compounds of formula (I).

As discussed above, Koza describes 7-substituted compounds, synthesized from sancycline, sulfuric acid and N-iodosuccinimide. The products produced in this reaction are a mixture of the 9-iodosancycline positional isomer, the 7-iodosancycline positional isomer, and 7,9-diiodosancycline.

The compounds described in Koza are a mixture of isomers and does not teach or suggest Applicants' tetracycline compounds, which are substantially free from positional isomers. Applicants' compounds, methods, and pharmaceutical compositions would not have been obvious to an ordinarily skilled artisan in view of Koza, because Koza does not describe methods to synthesize tetracycline compounds substantially free of positional isomers as claimed by Applicants.

Therefore, Applicants respectfully request that this rejection of claims 1-30, 32-45 and 47-64 under 35 U.S.C. § 103(a) be withdrawn.

SUMMARY

Cancellation of and/or amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The cancellation of and/or amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The amendments made to the claims are not related to any issues of patentability.

In view of the above remarks and amendments, it is believed that this application is in condition for allowance. If a telephone conversation with Applicant's Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call Elizabeth A. Hanley, Esq. at (617) 227-7400.

Date: February 10, 2003

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

28. [Amended] The compound of claim 27, wherein said 4-amino substituent is dialkylamino.

29. [Amended] The compound of claim 28, wherein said dialkyl amino group is dimethylamino.

32. [Amended] The compound of claims 1 ~~or 31~~, wherein said compound is at least 75% free of positional isomers.

47. [Amended] The method of claim 37 ~~or 46~~, wherein said tetracycline responsive state is a bacterial infection.

52. [Amended] The method of claim 37 ~~or 46~~, wherein said compound is administered with a pharmaceutically acceptable carrier.

53. [Amended] The method of ~~any one of~~ claims 37 ~~or 46~~, wherein said compound is at least 75% free of positional isomers.

58. [Amended] A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 ~~or 31~~, and a pharmaceutically acceptable carrier.